

Amendments to the Specification:

Note: paragraph numbers in the instruction refer to numbering of the published US application.

Replace the paragraph [0016] beginning on page 3, line 37 with the following:

U.S. Pat. No. 5,929,304 describes the expression of some lysosomal enzymes in tobacco plants. The enzymes are produced essentially in leaf by plants transformed via the use of vectors containing the MeGa promoter (deriving from the tomato HMG2 promoter) or the cauliflower mosaic virus (CaMV) 35S promoter. U.S. Pat. No. 5,929,304 reports, among the promoters indicated as useful in carrying out the invention, besides the above cited ones, also the rbcS promoter, the chlorophyll-binding a/b protein, the AdhI promoter and the NOS promoter. According to the teachings of this latter patent, the promoter used may be constitutive or inducible. In-leaf expression of enzymatically active human $[\square]\alpha$ -L-iduronidase is described in all the examples reported in the patent. The expression occurs following the transformation of tobacco plants with vectors containing, besides the sequence coding for the desired enzyme, the mechanically inducible MeGA promoter, or the constitutive 35S promoter, respectively.

Replace the paragraph [0023] beginning on page 6, line 25 with the following:

Pat. Appln. WO-A-00/04146, it being actually not aimed to enzyme expression, neglects several problems of fundamental relevance related to the stability of the exogenous protein expressed. In fact, the utmost stability of lactoferrin and the fact that in lactoferrin the presence of non-natural glycosidic chains does not influence protein folding and function, definitely bars the use of the system disclosed in Pat. Appln. WO-A-00/04146 from effectively expressing enzymes exhibiting a correct folding and being functionally equivalent to the native enzyme. Moreover, it is known that in the case of the acid $[\square]\beta$ -glucosidase the glycosylation of the first of the five glycosylation sites in the enzyme is crucial to the generation of an active

enzyme; said function pertains to the third glycosylation site in the case of α -galactosidase A, and in the case of acid β -glucosidase, the second glycosylation site is the one crucial to the generation of the mature enzyme.

Replace the paragraph [0025] beginning on page 7, line 23 with the following:

Plants lack the targeting system based on mannose-6-phosphate, do not possess MPRs and do not appear to produce phosphorylated glycans. Since lysosomal enzymes function in an acidic environment ($\text{pH} < 4$) and are unstable at higher ($> \text{ or } = 7$) pH values, the pH (5.8) of the plant (extracellular) apoplastic compartment makes the secretion of said enzymes in said compartment ideal for their stability. Although it is inferable that human lysosomal glycoproteins may be secreted in the apoplastic space (which would be particularly suitable for the storage of lysosomal enzymes), it does not follow that the system disclosed in the ~~above cited~~ above cited Patent Application be able to vehicle lysosomal enzymes in the apoplastic space of the seed storage tissue. For the abovementioned reasons, this localization could provide stability to expressed enzymes; in fact, an accurate localization of the lysosomal enzymes inside plant tissues is of fundamental importance for the stability of the produced enzyme.

Replace the paragraph [0047] beginning on page 12, line 6 with the following:

FIG. 7 reports the results of Northern analysis performed on RNA extracted from immature seeds (Days After Pollination, DAP, 20) of tobacco lines, transformed with the plasmid of FIG. 3 and tested positive at PCR control for gene presence detection, reported in FIG. 6. Total RNA extracted with the Trizol® method was loaded ($10 \mu\text{g/well}$) on agarose gel, subjected to electrophoresis, transferred on a nylon membrane and hybridised with a radioactive probe obtained by amplifying a human glucocerebrosidase gene fragment. Total RNA extracted from transgenic plants was loaded in lanes 1 to 8; C- is the negative control consisting of total RNA of a wild-type tobacco plant, C+ is the positive control consisting of total RNA

(15[] μ g) extracted from human placenta. The dimensions of the underlined band correspond to those expected for the messenger RNA (mRNA) of the GCB gene. The gene is not transcribed in plants 5, 6 and 8.

Replace the paragraph [0102] beginning on page 24, line 20 with the following:

The solution was filtered with filters of 0.2 μ m porosity, and the glucocerebrosidase partially purified by removing proteins of a <30 KDa molecular weight by centrifugation in ~~Centricon~~CENTRICON 30 column (~~Amicon~~AMICON).

Replace the paragraph [0104] beginning on page 24, line 29 with the following:

The elution fractions were reunited and filtered in ~~Centricon~~CENTRICON 30 to remove salt.

Replace the paragraph [0122] beginning on page 28, line 21 with the following:

The GAA gene coding for human acid [] β -glucosidase was cloned deleted of the region encoding the signal peptide, by RT-PCR technique, from mRNA purified from placenta, with the primers having sequences SEQ ID NO 14 and 15. The gene, in its structural portion deleted of the signal peptide as well (i.e. deleted of nucleotides 1-426 of SEQ ID NO 12) and of the poly-A site (not amplified by said primers) was isolated, amplifying the DNA having SEQ ID NO 12 starting from nucleotide 427 with the same primers, and cloned in pGEM®-T (Promega) to form the plasmid named pGEM-GLA. The primers designed for the amplification add the restriction site EcoRV to 5' and to 3'. The natural gene obtained, which at sequence control tested identical to the published one (Hoefsloot L. H. et al., 1988, EMBO JOURNAL 7(6), 1697-1704) in the portion encoding the mature peptide, was cloned in a vector analogous to that named pPLT2100 of example 1 under control of the PGLOB promoter to form the plasmid named pPLT4200 (FIG. 5). After accurate